

## **REMARKS**

The Applicants thank the Examiner for the examination to date and respectfully request reconsideration of the present application in view of the foregoing amendments and the reasons that follow.

### **I. Substance of the Interview**

The Applicants appreciate the courtesy extended by Examiners Barham and Wax in conducting an interview with the Applicants' representative on February 1, 2010. During the interview, the previously filed arguments and amendments were discussed.

### **II. Status of the Claims**

Independent claim 14 is amended for editorial changes to further clarify the claim language. Specifically, the claim recites that the aqueous dispersion comprises pioglitazone hydrochloride and a specific **core**-coating material. Support therefor can be found in, *inter alia*, Examples of the present Specification. The Applicants note that since the January 10, 2010 amendment has not been entered by the Office, the Applicants have reinstated the "and/or" recitation to replace the previously non-entered amendment "and." A detailed discussion related thereto is provided in the next section. New claims 21 and 22 are added to recite a specific embodiment of the core as recited in claim 14. Support therefor can be found in, *inter alia*, p. 15, lines 11-24 of the present Specification. No new matter is introduced, and claims 14-22 are currently pending to be examined on their merits.

### **III. Written Description**

According to the Advisory Action mailed February 23, 2010, the Office has not entered the amendment filed January 10, 2010 because the amendment allegedly raises written description issues. Advisory Action, p. 2. Specifically, during the interview, the Examiners expressed concern with the amendment to the hydroxypropyl cellulose, particularly the amendment of the claim language to "and" from "and/or."

While the Applicants maintain the arguments already set forth in the January 10, 2010 Reply, the Applicants reinstate the claim language prior to the non-entered amendment “and/or” to allay the Office’s concern with no literal support therefor from the present Specification. At the outset, one of ordinary skill in the art can appreciate that the term “and/or” refers to “one or more.” In other words, the present Specification provides support for **both** scenarios: (1) “either or” and (2) “both.” Specifically, the viscosity of the hydroxypropyl cellulose as recited in present claims 14 and 21 fulfills the values at either the 5% (w/v) level or the 2% (w/v) level or at **both** levels. Thus, while the Applicants maintain that the Office has not established any evidence that the presently claimed core-coating material can be reached based on the teachings of Cutie and Yano, alone or in combination, the Applicants hereby reinstate the previous claim language merely to allay the Office’s concern with literal support from the Specification. The Applicants believe all of the Office’s concern with respect to written description is addressed, and if the Office has any other issue with respect to same, the Applicants respectfully request the Office to explicitly state it on record. A discussion regarding the teachings of Cutie and Yano and the present claims is provided below.

Thus, the Applicants respectfully submit that the present claims are fully supported by the present Specification.

#### **IV. Claim Rejections – 35 U.S.C. § 103**

Claims 14-17 and 20 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over WO 01/82875 (“Cutie”) in view of US 5,547,683 (“Yano”). Claims 14-17 and 20 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over US 2004/0106660 (“Kositprapa”) in view of Yano<sup>1</sup>. Claims 14 and 18-20 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over US 2003/0060488 (“Sugiyama”) in view of Yano. Claims 14-20 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Sugiyama in view

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<sup>1</sup> The Applicants assume that the rejections with respect to claims 14-17 and 20 as stated on p. 4 of the Office Action are based on Kositprapa in view of Yano, with the latter being inadvertently omitted.

of Cutie or Kositprapa and further in view of Yano. The Applicants respectfully traverse all of these rejections.

(i) *Present claims are non-obvious over the teachings of Cutie and/or Yano*

Cutie does not teach or suggest every element recited in independent claims 14 and 20. Specifically, as acknowledged by the Office on p. 3 of the Office Action, Cutie does not teach at all the specific coating material as presently claimed – Cutie merely discloses that either the core or the first layer of a formulation, or both, may contain two active ingredients, metformin and pioglitazone (Cutie, p. 2, line 31 – p. 3, line 2). Moreover, Cutie does not teach or suggest at all coating a core with an **aqueous dispersion** of pioglitazone hydrochloride, as recited in present claims 14 and 20. In fact, to the extent that Cutie discloses a coating material, Cutie describes the material as an outer “shell” (e.g., Cutie, p. 7, lines 13-17), which is far different from the presently claimed “aqueous dispersion.”

Yano does not remedy these deficiencies. The Office relies on Yano merely because Yano in passing discloses using 5% HPC-SSL for a granule in one example. The Office then goes a step further and concludes that “it would have been obvious ...to substitute the low viscosity cellulosic polymer HPC-SSL or HPC-SL ... with predictable results.” Office Action, p. 4. The Applicants respectfully traverse. The Applicants respectfully submit that the Office’s assertion is based on mere hindsight and that the Office has misconstrued the teachings of Yano. In fact, contrary to the Office’s misconstrued teachings of Yano and Cutie, one of ordinary skill in the art would not have a reason to combine the teachings of Yano with those of Cutie.

**The Office has misconstrued Yano’s teachings**

The Applicants maintain the position as stated in the January 20, 2010 Reply that Yano does not remedy Cutie’s deficiencies. One would not have had a reason to combine the teachings of Yano with those of Cutie merely because Yano mentions “hydroxypropyl cellulose.” The

cellulose of Yano is used as a **binder** to facilitate **granulation** of particles, which is in a different field of endeavor from providing a coating on a core, as disclosed by Cutie.

At the outset, spraying a granulated particle with a cellulose **as a binder** (as in Yano) is **not the same** as coating a core with an aqueous suspension of the particle and the cellulose (as in the present invention). A binder in granulation, as can be appreciated by one of ordinary skill in the art and by the disclosure of Yano (*see* col. 6, lines 13-44) is to **bind** or **agglomerate** particles (“it is **necessary** to control the granulation ...by **binding** together uniformly coated particles.”). By contrast, the “shell” of Cutie has little to do with granulation. Similarly, the presently claimed methods have little to do with coating the pioglitazone hydrochloride with the “**core-coating material**” (i.e., the coating material is to coat the “**core**,” as reflected in the name), much less to bind or agglomerate the pioglitazone hydrochloride with that material.

The Office’s misunderstanding of Yano’s teachings is further evidenced on p. 4 of the Office Action and p. 2 of Advisory Action. Contrary to the Office’s assertion in the Office Action, the method of “coating” of Yano is **not** the same at all as the “coating” in the present claims. Further, in contrast to the Office’s assertion in the Advisory Action, the cellulosic polymer in Yano does **not** “allow ease of control of *coatings*” (emphasis added). *See* line 8 on p. 2 of Advisory Action. Rather, Yano in col. 4, lines 24-33 discloses that such cellulose **binder** permits “easy control of **granulated particles**.” The Office’s has misanalogized the granulated particles of Yano with the coating of the present claims.

Yano’s Example 1 (which is referenced by the Office on p. 3 of the Office Action) describes that a 5% HPC-SSL cellulose is sprayed to coat **the granulated particles** to facilitate the process granulation, and the coated particles are subsequently **dried** before any further process. Thus, if one were to follow the Office’s rationale to combine the teachings of the binder-coated granulated particles of Yano with the composition of Cutie, one would have combined a dried cellulose-coated granulated particle into the shell of Cutie. This is hardly the same as a step of coating a core with **an aqueous dispersion**, comprising-pioglitazone

hydrochloride and a core-coating material that is a cellulose, as recited in the present claims, and, in fact, is a separate step. Specifically, the dried cellulose-coated granulated particle of Yano would not be in an aqueous dispersion, and the cellulose binder of Yano would not be used to coat the core, much less a core being a sustained release preparation containing a biguanide, even less a core being sustained release preparation containing metformin hydrochloride. *See* new claims 21 and 22, respectively. Thus, claims 21-22 are separately patentable.

Additionally, as already provided in the January 20, 2010 Reply, in the presently claimed methods, HPC-SL and HPC-SSL are used as coating materials during pioglitazone coating and are selected for the purpose of rapid dissolution of pioglitazone, especially dissolution within the first 15 minutes of the dissolution test (*see e.g.*, ¶ [0010] and Examples in the present published Specification). In stark contrast to Yano's teachings, the presently claimed preparations are not intended, and do not need to undergo granulation, to achieve rapid dissolution. Such rapid dissolution based on the type of cellulose employed is unexpected based on Yano's teachings that can accomplish its goal via an entirely different process (i.e., granulation). In fact, Yano's teachings could not be expected to manifest the desirable dissolution properties as a result of these specific celluloses. Thus, such unexpected results of the presently claimed preparations rebut any *prima facie* case of obviousness. Further, the Office's assertion is mere hindsight. *Sanofi-Synthelabo v. Apotex, Inc.* 550 F.3d 1075, 1088 (Fed. Cir. 2008) (holding that the application of hindsight is inappropriate where the prior art does not suggest the properties and advantages).

Thus, contrary to the Office's position, one of ordinary skill in the art would not have had a reason to combine the teachings of Yano with those of Cutie. Even assuming, *arguendo*, that these teachings were combined, any possible case of *prima facie* obviousness would be rebutted by the unexpected results set forth above.

(ii) Present claims are non-obvious over the teachings of Kositprapa, Cutie, Sugiyama, and/or Yano

The Office's rejections based on Kositprapa in view of Yano and Sugiyama in view of Cutie/Kositprapa and further in view of Yano are similar to those with respect to Cutie in view Yano, and the Applicants respectfully traverse the same.

As already explained in the April 24, 2009 Reply and as acknowledged by the Office on pp. 5-7, Sugiyama and Kositprapa do not teach and suggest every element recited in the present claims. Specifically, neither Sugiyama nor Kositprapa teaches or suggests the recited aqueous dispersion that contains the specific cellulose. Similarly to the rejection regarding Cutie and Yano, the Office relies on Yano to remedy the deficiencies. However, the Applicants respectfully submit that there is no "synergistic" or "enhanced" effect suggested by any of these teachings (*see* Office Action, p. 9), contrary to the Office's statement. In fact, similar to the explanation set forth above, one of ordinary skill in the art would not have had a reason to combine the teachings of Yano with those of Sugiyama and/or Kositprapa. Furthermore, even assuming, *arguendo*, that these teachings were combined, any possible case of *prima facie* obviousness would be rebutted by the unexpected results set forth above. Thus, the present claims are non-obvious over the teachings of Kositprapa, Cutie, Sugiyama, and/or Yano.

Therefore, the Applicants respectfully request that the rejections be withdrawn.

**CONCLUSIONS**

The Applicants believe that the present application is now in condition for allowance and thus respectfully request favorable reconsideration of the application.

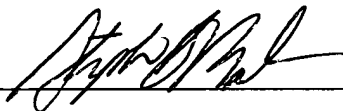
The Office is invited to contact the undersigned by telephone if a telephone interview would advance the prosecution of the present application.

The Office is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, the Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorize payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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